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The effectiveness of multicomponent lifestyle interventions for supporting weight loss in adults taking antipsychotic medication: a literature review.

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Title Page

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The effectiveness of multicomponent lifestyle interventions for supporting weight loss in adults taking antipsychotic medication: a literature review.

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Abstract:

Antipsychotic medication is effective in reducing psychotic symptoms but use is associated with weight gain. Weight gain is associated with an increased risk of a number of life threatening health conditions. Multi-component lifestyle interventions are the recommended non-pharmacological way of tacking weight gain and its consequences. This review summarises the evidence for the effectiveness of multi-component lifestyle intervention in reducing weight and waist circumference in adults taking antipsychotics. The review of eight studies found that such approaches are effective, however multiple factors affect success, for example tailoring of information to the cognitive abilities of participants and the use of individual combined with group approaches. Eight studies were reviewed. There were some unexpected results within studies, where some control groups lost weight or decreased waist circumference as well as intervention groups. Reasons for significant weight change in control groups was attributed to possible access to weight loss activities outside of the intervention programmes. Adherence to intervention programmes was also important for success. Nurses who support antipsychotic users to lose weight should promote multi-component approaches that are tailored to the specific needs of this group.
183 words

Key points

- Weight gain is a major concern for people prescribed antipsychotics, affecting treatment adherence and heightening risk of a number of life threatening physical health conditions.
- Multi-component lifestyle interventions, comprising diet and exercise educational and behavioural interventions are the nationally recommended first line approach to weight gain.
- There have been a number of randomised control trial (RCT) studies of multi-component lifestyle interventions for people taking antipsychotics.
- Successful weight loss is possible if interventions contain both group and individual elements and if the content is tailored to this specific population.
- More research is needed to compare effectiveness of multi-component interventions between populations taking antipsychotics, namely people with different degrees of obesity, levels of cognitive functioning and ethnicity.

List of Tables and Figures:

Introduction

Antipsychotic medications are effective for the treatment and management of psychotic symptoms; however they often produce unpleasant side effects (Lally & MacCabe 2015). One of these includes weight gain (Bak et al, 2014). The mechanisms of antipsychotic related weight gain are thought to be associated with their effect on histamine, serotonin and acetylcholine metabolism (Richards & Bressington 2015). Adults taking antipsychotics long term have a reduced life expectancy due to the increased prevalence of obesity (Olfson et al, 2015), with a study by Chang et al, (2011) finding that men with schizophrenia's life expectancy was reduced by 14.6 years and women with schizoaffective disorders reduced by 17.5 years. Antipsychotic weight gain costs the healthcare system as well as the individual (Shrivastava & Johnston 2010). Experiencing weight gain can often lead to adults deciding to stop compliance with antipsychotic regimes (Eapen & John 2011). Antipsychotic regime non-adherence increases the frequency and duration of hospital admissions, and use of secondary care services (Marcus & Olfson (2008) and this can have a significant impact on health and wellbeing. Rege (2008) states that achieving an optimal balance between effectiveness and weight maintenance in antipsychotic treatment is possible if appropriate intervention occurs. Obesity in this population is usually a result of lifestyle factors such as inactivity or poor diet (Gossage-Worrall et al. 2016), hence, this is a crucial area to target.

The consequences of obesity: metabolic syndrome, diabetes and cardiovascular disease can be reduced if weight is lost (Heald 2010). Pharmacological interventions are often used for weight loss, such as switching antipsychotics or the use of metformin (Shrivastava & Johnston 2010, Mizuno et al, 2014), however, non-pharmacological interventions may be more appealing to service users as there is not the same risk of further medication side effects (Caemmerer et al, 2012). A lifestyle-focused, health promotion approach to

physical wellbeing has been advocated within mental health services for several years although gaps in the provision of high quality physical healthcare for people with severe mental illness remain (McGuinness & Folan, 2016).

Multi-components lifestyle interventions are non-pharmacological interventions that are usually administered between 3-18 months (McCloughen & Foster 2011) composed of two or more elements such as diet modification and increased physical activity (McCloughen & Foster 2011). Previous systematic reviews have found that such approaches support weight loss in adult populations (Poobalan et al, 2009, Mitchell et al, 2014, Hassan et al, 2016). Recent reviews have found that multi-component interventions can reduce weight with serious mental illness (Olker et al, 2016, Naslund et al, 2017). The National Institute of Health and Clinical Excellence (NICE) guidelines on psychosis (2014a) advocate multi-component lifestyle interventions for excessive weight gain (NICE 2014b; 2015). However, a limited number of reviews have explored the effectiveness, specifically focusing on comparing service users who use antipsychotics (Olker et al, 2017, Bushe et al, 2009; Murray et al, 2017) and aiming to inform mental health nursing practice.

Aim

The aim of this review is to explore the success of multi-component lifestyle interventions in reducing obesity in adult populations on antipsychotics, focusing on weight, BMI and waist circumference as primary outcomes.

Methods

A search was undertaken using the following databases; Cumulative Index to Nursing and Allied Health Literature (CINAHL), Medline, Web of Science and PsycInfo. Search terms were derived using a PICO approach (Population, Intervention, Comparator and Outcome): multi-component lifestyle interventions (Intervention) for supporting weight loss

(Outcome) in adults on antipsychotic medication (Population) in comparison to non-intervention (Comparator). The search process is shown in a PRISMA flow diagram (Moher et al, 2009) in ***Figure 1***. The inclusion criteria for the studies were: published in English language with adults (18 years and above) who were currently on antipsychotic medication. Only randomised-controlled trials (RCTs) were included. The included study papers were reviewed in full and summarised using a data extraction form. Study quality was assessed using the Critical Appraisal Skills Programme (CASP; 2013) checklist for RCTs. Additionally, the Cochrane Handbook risk of bias tool (Higgins & Green 2011) was used to assess of bias and study validity.

Results

8 papers were included, describing 8 RCT studies. ***Table 1*** provides a summary of study characteristics. 55.7% of the participants were female and 44.3% were male. The mean ages within studies ranged from 26.3 to 48.8 years. Intervention and control groups characteristics were similar at the start of the trials aside from Ratliff et al, (2012) where the baseline antipsychotic dose was statistically different between the groups. Selection criteria for study participants were that they had to be taking antipsychotics and had experienced weight gain. Doses for specific drugs or duration of their use were not reported, apart from in Wu et al, (2007) where all participants had been on at least 300mg clozapine for over a year. Attux et al, (2013) listed the numbers of participants on different antipsychotics but found no difference in results between those on first generation or second generation drugs.

Interventions

Interventions ranged from 2 and 12 months in duration and the mean intervention duration was 4 months. Wu et al, (2007) was the only study in which diet was fully controlled as

their participants were inpatients. All other studies took place in the community. Six studies provided exercise sessions (Wu et al, 2007, Wu et al, 2008, Usher et al, 2012, Green et al, 2014, Masa-Font et al, 2015, Green et al, 2015). Two studies did not provide exercise sessions but encouraged physical activity through psychoeducation (Attux et al, 2013) or a combination of psychoeducation and Contingency Management (CM), which is a behavioural technique whereby participants are offered financial incentives for either buying healthy food, losing weight or attending the programme (Ratliff et al, 2013).

Five studies tailored their intervention for the specific population. Usher et al, (2012) adapted their intervention to account for the cognitive complications that can occur with a diagnosis of schizophrenia, for example, differing levels of literacy, difficulty in conversation and impaired memory. They also added visual representations of the training sessions to aid learning. Green et al, (2014) equally adapted their intervention to meet the cognitive needs of participants, adjusting the pace and breaking down information and tasks. Green et al, (2015) did the same and additionally provided psychoeducation around the effects of antipsychotics. Ratliff et al, (2012) used a lifestyle intervention that was specifically created for individuals with mental illness. It assumed no knowledge of the discussed topics and used simplified terms. The programme that Attux et al, (2013) used was developed for individuals on antipsychotics and included a session to support motivation and self-esteem. Adapting the intervention ensures it is as appropriate for the population as possible.

Intervention adherence

Data on treatment adherence is crucial as this provides us with information on intervention acceptance by participants (Zhang et al, 2014). Attrition can create bias within a study, if results favour participants who stay, leading to underestimation about the potential complications of the intervention (Peterson et al, 2012). Only one study had 100% adherence/attendance within their intervention. This was Wu et al, (2007) and was likely to be

achieved because the intervention was carried out within an inpatient environment. Furthermore, studies that include social support have higher intervention adherence rates (Lemstra et al, 2016). This was true within the studies by Attux et al, (2013) and Green et al, (2014), who invited families to come to intervention group sessions. Similarly, the study by Wu et al, (2007) required carers to support the physical activity component and intervention adherence was relatively high (55-74%). There is no specified point at which intervention attrition becomes an issue, but rather bias is introduced if there are differences in participants who left the intervention and the control group (Dumville et al, 2006). Ratliff et al, (2012) stated that one participant dropped out from each condition; however, there was no explanation for this. Usher et al, (2012) reported that two participants left due to medical reasons, but did not state what these were and what group they were randomised to. Although Attux et al, (2013) provided detail on most drop-outs; there were a total of 8 participants where reasons for dropping out were unknown. Within these studies, there is an unclear risk of attrition bias. In the study by Masa-Font et al, (2015) information on attrition was provided; however, there was a death in the intervention group and details of this was not provided. Masa-Font et al, (2015) had the lowest intervention adherence; this was between 42.6-58%. This was the only study where the intervention group gained weight. A recent meta-analysis of weight loss intervention studies across all populations by Lemstra et al, (2016) explains this pattern simply: if participants do not adhere to the weight loss interventions then they will not lose weight, and may even gain it.

Weight loss

Figure 2 shows the changes in weight (kg) within the intervention and control groups. The intervention group with the greatest statistical significant weight loss was Green et al, (2015) after the initial intervention phase (4.2354 kg). Although weight loss after the maintenance phase was larger (4.887 kg) it was not significantly different

(95%CI). This result suggests that the intensity and greater number of sessions may be a key component of success within these interventions. Attux et al, (2013) found that significant weight loss (1.15 kg) occurred at their last measurement of 3 months' post intervention but not immediately at intervention end where weight loss was insignificant (0.4 kg)($p<0.05$). This highlights that the effects of lifestyle interventions may not be immediate, emphasizing the need for post-intervention measurements, to see how outcomes develop over a longer period. Participants in the intervention by Wu et al, (2007) lost a mean of 1.3 kg, suggesting that even a program simply consisting of calorie constriction and walking may support weight loss in an inpatient environment ($p<0.05$). In the study by Ratliff et al, (2012) only weight loss in the intervention group receiving financial incentives for choosing healthy food was significant (2.54 kg)($p<0.02$). The other two intervention groups (rewarding for attendance or weight loss) lost weight but not significantly when compared to controls. This suggests that lifestyle interventions combined with CM rewarding for behaviour change may be the most effective in this population. The nurse-led intervention by Usher et al, (2012) produced the least weight loss (0.74 kg) and was not statistically significant ($p<0.05$). Usher et al, (2012) provided control participants with a copy of the intervention education booklet, and here the control group weight also decreased. This suggests that even minimal intervention such as educational booklets may influence behaviour change and weight loss. The control group in the study by Green et al, (2014) lost 0.3kg but this was not explained. However, in Green et al, (2014) this did not change their BMI. Green et al, (2015) found that the intervention group lost 2.6 kg more than the control group after the maintenance phase. However, there was no significant difference in weight change between the groups (95% CI). This was attributed to the opportunity control group participants had to engage in other weight-loss methods. Nonetheless, at the end of the initial intervention the control group had an increase in weight (0.96 kg).

Only one study (Attux et al, 2013) presented information about how long weight loss was maintained post- intervention. They found that weight loss was not significant immediately post-intervention but 3 months' post-intervention it was significant. The study by Green et al, (2015) was followed up in a separate study. In contrast, at one-year post-intervention, weight change between intervention and control group participants was statistically insignificant (Green et al, 2016). This suggests that whilst multi-component interventions have the potential to be beneficial to the health of an adult on antipsychotic medication; it is still unclear how long these positive effects last.

BMI

Figure 3 shows the BMI changes (kg/m2) within the intervention and control groups.

All studies within the review measured BMI. However, three studies (Ratliff et al, 2012; Green et al, 2014; Green et al, 2015) did not report BMI results for all conditions so have not been included in the comparison chart. Six studies found a statistical difference between the intervention and control groups for BMI. In all the studies but Usher et al, (2012) and Masa-Font et al, (2015) the BMI of the intervention group decreased yet increased within the control group. Usher et al, (2012) found that BMI decreased in both the intervention (0.25 kg/m2) and control (0.06 kg/ m2) group. As stated above, this difference was not statistically significant ($p>0.05$). The study by Masa-Font et al, (2015) was the only one where the intervention group gained weight and the control group lost weight. They found that the control group's BMI decreased significantly (0.23kg/m2) in comparison to the intervention group where BMI increased on average (0.04kg/m2) ($p<0.05$). They attributed this result to the fact that that control group participants may have engaged in other weight loss programmes and the low adherence rates within the intervention group.

Waist circumference

Waist circumference measurements are effective long term measures of weight loss maintenance post-interventions (Millstein 2014). Six studies measured waist circumference. ***Comparisons between intervention and control groups are presented in Figure 4.*** Wu et al, (2007) and Wu et al, (2008) were the only studies to find statistical significance in waist circumference between the intervention and control groups ($p<0.05$). In three studies waist circumference, decreased in the intervention group and increased in the control group (Wu et al, 2007, Ratliff et al, 2012, Attux et al, 2013). However, in the studies by Wu et al, (2008), Usher et al, (2012) and Masa-Font et al, (2015) this was not the case. Wu et al, (2008) reported an increase in waist circumference in both the intervention (0.1 cm) and control (2.2 cm) groups. Usher et al, (2012) found a waist circumference decrease in both the intervention group (1.23 cm) and control group (0.15 cm). Masa-Font et al, (2015) found that the control group's waist circumference decreased (0.018 cm) and the intervention group waist circumference increased (0.98 cm).

In addition to waist circumference Wu et al, (2007) measured body fat percentage, hip circumference and waist-to-hip ratio. They found a statistical difference in hip circumference between the intervention (3.3 cm) and control group (0.3 cm) at the intervention end ($p<0.05$). For waist-to-hip ratio they did not find a significant difference between the intervention (0.1) and control group (0.1). Similarly, they found that body fat percentage was not significantly lower within or between the intervention (1.3%) and control (1.3%) groups. Nevertheless, these parameters decreased with intervention and increased with non-intervention.

Risk of bias

A summary review of risk of bias is shown in Table 2. According to the Cochrane criteria (Higgins & Green 2011), all the studies included in this review had a risk of performance bias because the nature of the intervention was not concealable. Additionally, methods of

randomisation were not stated in two studies (Wu et al, 2007; Usher et al, 2012). Allocation concealment information was not reported in three studies (Wu et al, 2007; Ratliff et al, 2012; Attux et al, 2013) so risk of selection bias was unclear. One study did not provide the data of all outcomes for the insignificant results (CM-weight and CM-attendance) whereas they did for the significant results (CM-behaviour) (Ratliff et al, 2012).

Discussion

This review has expanded upon the findings of previous reviews, which made the case for further investigation into similar interventions (Caemmerer et al, 2012, Bruins et al, 2014). We have included additional RCTs, exploring a wider range of interventions, focusing solely on weight change and updating the current evidence. Our findings are consistent with those of existing reviews regarding various non-pharmacological interventions on individuals on antipsychotics which found that intervention was successful for both weight loss and/or weight-gain prevention in comparison to control groups (Bonfoli et al, 2012, Caemmerer et al, 2012, Bruins et al, 2014). Our review has considered more anthropometric measures than previous reviews, to explore weight loss in greater depth.

Overall, when compared to a control group, adults taking antipsychotics lose weight when enrolled on multi-component lifestyle interventions. Combined mean weight change across the interventions was -2.72 kg (excluding those who didn't provide baseline weight in kg). This corresponded to a weight loss of 2.93% from baseline. Although weight loss is usually reported as at least 5% to be considered clinically significant (Lagerros & Rossner 2013), even small decreases in weight can induce corresponding reductions in physical health complications and early mortality (Alvarez-Jimenez et al, 2008, Bruins et al, 2014).

Current clinical guidelines on weight management (NICE 2014a) and schizophrenia (NICE 2015) encourage the use of multi-component interventions to support weight loss although

there is no specific guidance for interventions for antipsychotic weight gain. The evidence from this review suggests that interventions should be tailored, suggesting the benefit of an additional clinical guidance specifically for adults on antipsychotic medication. For example, a diagnosis of schizophrenia may mean that levels of concentration and comprehension abilities that need to be accounted for through intervention adaptations (Usher et al, 2012).

There is a lack of information in included studies about how long weight loss is maintained post-intervention, as only Attux et al, (2013) provided this information, finding that intervention end weight loss was not significant, but 3 months' post-intervention, weight loss was significant. The study by Green et al, (2015) was followed up in a separate study. In contrast, at one-year post-intervention, weight gain between intervention and control group participants was statistically insignificant (Green et al, 2016). This suggest that furth work must be done to track weight change and maintenance post-intervention. Masa-Font et al (2015) had the lowest intervention adherence of between 42.6 and 58%. Theirs was the only study where the intervention group gained weight. The recent meta-analysis by Lemstra et al, (2016) offers an explanation for this. They state that if participants do not adhere with weight loss interventions then they will not lose weight, and may even gain it. Interventions with family/social support had higher adherence rates. Hence, the involvement of family and carers may further encourage and provide motivation for participants to engage.

Studies characterised by a mixture of both an individual and group approach were more effective than studies that used only one of these components. Individual approaches allow for personal advice and specific goals to be created. Group approaches usually provide an element of social support and shared learning. . A combined approach provides a space where the benefits of both can be gained. Additionally, it appears that success can occur in both inpatient and outpatient settings. However, as only one study was conducted

in an inpatient setting, it would be premature to generalise these results to all inpatient environments.

Limitations

This review has limitations. It has focused on three primary outcomes: weight loss, waist circumference reduction and BMI reduction. More detail on the differences within the population taking antipsychotics should be accounted for, for example variation in doses of antipsychotics and brand of antipsychotics used and differentiation between age and duration of antipsychotic use between participants. Measuring the differing effects of these interventions with people with different degrees of being overweight and obesity, on different antipsychotics and of different ethnicities was not possible given current study information. Also, the multicomponent interventions reported here varied in duration and content. Whilst it is possible to summarise that such interventions work, there must be more analysis of the aspects of such interventions that are effective, and comparison between types of intervention. Additionally, as all studies included within this review were RCTs, the results may not be as representative of the naturalistic environment. It may be beneficial to include a qualitative element in future studies, in order to gain service users' insights into what worked and why. The intervention and data collection periods ranged from 3 to 12 months so future studies would benefit from measuring sustained weight loss over longer periods of time.

Conclusion

This review found that weight loss, BMI reduction and decreased waist circumference in adults taking antipsychotics is possible if multi-component interventions are adhered to. If multi-component lifestyle interventions provide tailored support then they have more potential to produce clinically significant weight loss. Further research is needed to explore

booster/maintenance interventions, monitor long term effects, intervention cost-effectiveness and compare the use of both tailored and longer interventions.

Practice Implications

For the included studies, limited weight loss within intervention groups was attributed to several factors: particularly lack of intervention adherence and use of interventions that were not tailored to the client's needs. It is crucial that all nurses are aware of the importance of offering antipsychotic users interventions that are appropriate for their treatment regimes and cognitive abilities. Nurses should ensure that they are supporting antipsychotic users to attend sessions. In a population where treatment adherence is an acknowledged concern, close attention should be paid to what motivates individuals on antipsychotics to commit or drop out of such treatment programmes.

3430 words

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Table 1: Summary of studies

Author & year of publication	Study location	Study aim & main measures	Number of participants, inclusion criteria, duration of study & control condition	Lifestyle intervention components	Method of data collection and analysis	Main findings
Wu *et al.* (2007)	Taichung, Taiwan	**Study aim** – To assess the efficacy of dietary control and exercise among obese inpatients with schizophrenia being treated with clozapine. **Measures** – BMI, body weight, body fat composition, waist-to-hip ratio (waist circumference and hip circumference) and fasting blood test (glucose, triglyceride, cholesterol, prolactin, cortisol and insulin).	**Number of participants** – 53 (Intervention group – 28 + Control group – 25). **Inclusion criteria** - a diagnosis of schizophrenia, aged 18 to 65 years old, taking at least 300 mg of clozapine orally per day for at least a year and having a BMI greater than 27 kg/m2. **Duration of study** – 6 months **Control condition** – Clozapine treatment as usual	6 months of dietary intervention. 6 months of exercise for an hour 3-times a week.	**Data collection** – Data collected at baseline, 3 months and 6 months. **Data analysis** – Statistical analyses using ANCOVA based on a general linear model.	The intervention group participants experienced a statistically significant decrease in weight (kg). This additionally occurred with BMI (5.4% reduction), hip circumference and waist circumference (both reduced by 3.3 cm) during the trial and post-at intervention end.
Wu *et al.* (2008)	Hunan Province, China	**Study aim** – To evaluate the effects of a lifestyle intervention and metformin both alone and in combination for antipsychotic-induced weight gain and abnormalities in insulin sensitivity. **Measures** – BMI, waist circumference and insulin levels.	**Number of participants** – 64 (Lifestyle intervention group – 32 + Control group – 32). **Inclusion criteria** - aged 18 to 45, with a first psychotic episode of schizophrenia, had gained more than 10% of their predrug body weight within the first year of treatment with a targeted antipsychotic agent—clozapine, olanzapine, risperidone, or sulpiride, had to have relatively stable improvement in psychotic symptoms, and be taking only 1 antipsychotic agent, whose dose had not changed by more than 25% over the past 3 months. **Duration of study** – 3 months **Control condition** – Placebo only	3 months of psychoeducation about food and physical activity and exercise sessions Participants engaged in endurance exercise every day for 30 minutes for the first week and then moderate exercise for 30 minutes' minimum daily.	**Data collection** – Data collected at baseline, 1 month, 2 months and 3 months. **Data analysis** – Statistical analyses using ANCOVA to compare all continuous variables and x^2 analysis was used for categorical variables.	Intervention participants had a statistically significant decrease in all body weight parameters in comparison to the placebo group. Here, the placebo group has a significant increase in all body weight parameters.

Ratliff *et al.* (2012)	New Haven, USA	**Study aim** – To evaluate the feasibility of using contingency management (CM) to promote weight loss in individuals with serious mental illness over 2 months. **Measures** – BMI, waist circumference, weight, plasma glucose levels, plasma insulin levels, glycosylated haemoglobin.	**Number of participants** – 30 (Lifestyle intervention group with CM via attendance – 10 + Lifestyle intervention group with CM via weight loss - 10 + Waitlist control/ CM for behaviour group – 10). **Inclusion criteria -** aged 18 to 70 years with SMI who were on a stable dose of antipsychotics for at least 1 month and self-reported weight gain 6 5% over the past 5 years **Duration of study** – 2 months **Control condition** – Waiting list	Lifestyle intervention group with CM via attendance – The lifestyle intervention consisted of weekly, hour-long group sessions to provide knowledge on diet and physical activity. Participants received either 1) attendance, 2) weight loss, 3) behaviour change.	**Data collection** – Weight was measured weekly after baseline. All other outcomes were measured at baseline and at the 2 months. **Data analysis** – Statistical analyses using ANCOVA and Spearman's correlation coefficient.	Participants in the CM attendance and CM weight group lost a mean of 1.16 kg and 1.23 kg receptively, while subjects in the CON gained a mean of 0.68 kg. Participants in the CM behaviour group lost a mean of 2.54kg, which was a statistically significant in comparison to the control group.
Usher *et al.* (2012)		**Study aim** – To assess the effectiveness of a nurse-led intervention on weight gain in people with serious mental illness prescribed and taking second generation antipsychotic medication. **Measures** – BMI (Height + Weight), medication compliance.	**Sampling strategy** – Purposive sampling through advertisement in outpatients. **Number of participants** – 101 (Lifestyle intervention group – 51 + Control group – 50). **Duration of study** – 3 months **Control condition** – Education booklet	One-hour group sessions every week for three months. The group session included education on different healthy lifestyle topics. After the group there was a 30 minutes of physical activity.	**Data collection** – Data collected by the researchers at baseline and 3 months. **Data analysis** – Statistical analyses using Chi-squared texts, Fisher's exact tests, unpaired t-tests and non-parametric Mann-Whitney Wilcoxon U-tests.	Results were not statistically significant. The intervention group had a decrease in weight at intervention end of -0.74 kg. However, the control group also had a decrease in weight, this was -0.17 kg at intervention end.

Attux *et al.* (2013)	Sao Paulo, Brazil	**Study aim** – To test the efficacy of a 12-week group behavioural and psychoeducation interventions on weight gain management. **Measures** – BMI, body weight, waist circumference, systolic BP, diastolic BP and fasting blood test (glucose, triglyceride, cholesterol and insulin levels).	**Number of participants** – 160 (Intervention group – 81 + Control group – 79). **Inclusion criteria**- aged between 18 and 65, using any antipsychotic in the past three months, presenting a diagnosis on the schizophrenia spectrum, motivated to lose weight or have showed some concern about weight gain. **Duration of study** – 6 months **Control condition** – Treatment as usual	3 months of one-hourly weekly sessions to discuss topics such as lifestyle and diet and behaviour techniques i.e. diaries.	**Data collection** – Data collected at baseline, 3 months and 6 months. **Data analysis** – Statistical analyses using ANOVA for comparison of the groups and two sided t-tests and chi-square tests to analyse the differences between groups at baseline and follow up.	At the intervention end, intervention group participants had a weight loss of 0.48 kg while the control group experienced an increase of 0.48 kg. This was not statistically significant at 3 months' post intervention, the intervention group lost a statistical significant weight loss of -1.15 kg.
Green *et al.* (2014)	Oregon, USA	**Study aim** – To test the efficacy of a 12-week weight reduction intervention for overweight individuals taking antipsychotic medications. **Measures** – Height, weight, blood pressure.	**Number of participants** – 36 (Intervention group – 18 + Control group – 18). **Inclusion criteria** - BMI of 25–44.9) aged over 18 years who had been taking at least one antipsychotic medication at any consistent dose for a minimum of 30 days at the time they were identified. **Duration of study** – 3 months **Control condition** –Treatment as usual	3-month intervention composed of a moderate calorie restriction, increase in healthier food, increase in physical exercise and daily use of a food diary.	**Data collection** – Data collected by blinded staff at baseline, and a week post-treatment. **Data analysis** – Statistical analyses using ANOVA.	Here there was a statistically significant decrease in the weight of intervention from 213.3 to 206.6 pounds. Control group participants had a relatively unchanged weight. BMI results mirrored this.
Masa-Font *et al.* (2015)	Barcelona, Spain	**Study aim** – To evaluate the effectiveness of a physical activity and diet to change the amount of physical activity, BMI and waist circumference in patients with severe mental illness. **Measures** – Level of physical activity, BMI, waist circumference, cholesterol, triglycerides, glucose, metabolic equivalent units (METS) dietary habits and quality of life.	**Number of participants** – 332 (Intervention group – 169 + Control group – 163). Inclusion criteria - diagnosed with a schizophrenic, schizoaffective or bipolar disorder, undergoing treatment with an antipsychotic drug for at least 3 months prior to enrollment, with low Physical Activity, BMI values equal to or greater than 25 **Duration of study** – 3 months **Control condition** – Treatment as usual	Twice-weekly physical activity interventions (between 40-60 minutes) and twice-weekly diet education sessions (20 minutes each).	**Data collection** – Data collected by blinded staff at baseline and at 3 months. **Data analysis** – Statistical analyses using ANOVA.	At 3 months, the BMI decreased significantly more in the control group, by 0.26 kg/ m^2 than in the IG. There were no significant differences in the waist circumference.

Green *et al.* (2015)	Oregon, USA	**Study aim** – To assess where a tailored lifestyle intervention for individuals with serious mental illness produces weight loss and lowered diabetic risk. **Measures** – Blood pressure, BMI (height and weight), and fasting blood sample (insulin, plasma glucose, triglycerides and cholesterol).	**Number of participants** – 200 (Intervention group – 104 + Control group – 96). **Inclusion criteria** -adults (age $18) taking antipsychotic agents for over 30 days prior to enrollment and with a BMI over 27. **Duration of study** – 12 months (Initial intervention – 6 months + Maintenance intervention – 6 months). **Control condition** – Treatment as usual	**Initial intervention** – 6 months of weekly 2-hour group meetings to support self-management and diet changes (DASH diet) with 20 minutes of physical activity. **Maintenance intervention** – 6 months of group sessions focusing on motivation enhancement. Additionally, monthly individual telephone sessions to support problem-solving.	**Data collection** – Blinded staff collected data at baseline, 6 months and 12 months. **Data analysis** – Statistical analyses using one way ANCOVA and multiple logistic regression.	Intervention participants lost 4.4 kg more than control participants from baseline to 6 months. Here control groups participants experienced an increase in weight (kg). Intervention participants lost 2.6 kg more than control participants from baseline to 12 months (intervention end).

Table 2: Risk of Bias

Risk of bias domain	Wu *et al.* (2007)	Wu *et al.* (2008)	Ratliff *et al.* (2012)	Usher *et al.* (2012)	Attux *et al.* (2013)	Green *et al.* (2014)	Masa-Font *et al.* (2015)	Green *et al.* (2015)
Random sequence allocation (selection bias)	?	+	+	?	+	+	+	+
Allocation concealment (selection bias)	?	+	?	+	?	+	+	+
Blinding of participants (performance bias)	-	-	-	-	-	-	-	-
Blinding of outcome assessment (detection bias)	-	+	?	-	-	+	+	+
Incomplete outcome data (attrition bias)	+	?	?	?	?	+	?	+
Selective reporting (reporting bias)	+	+	-	+	+	-	+	?
Lack of intent-to-treat analysis	-	+	+	-	+	+	+	+

Key: + = Low risk of bias? = Unclear risk of bias, - = High risk of bias.

Figure 1 Selection process flow chart

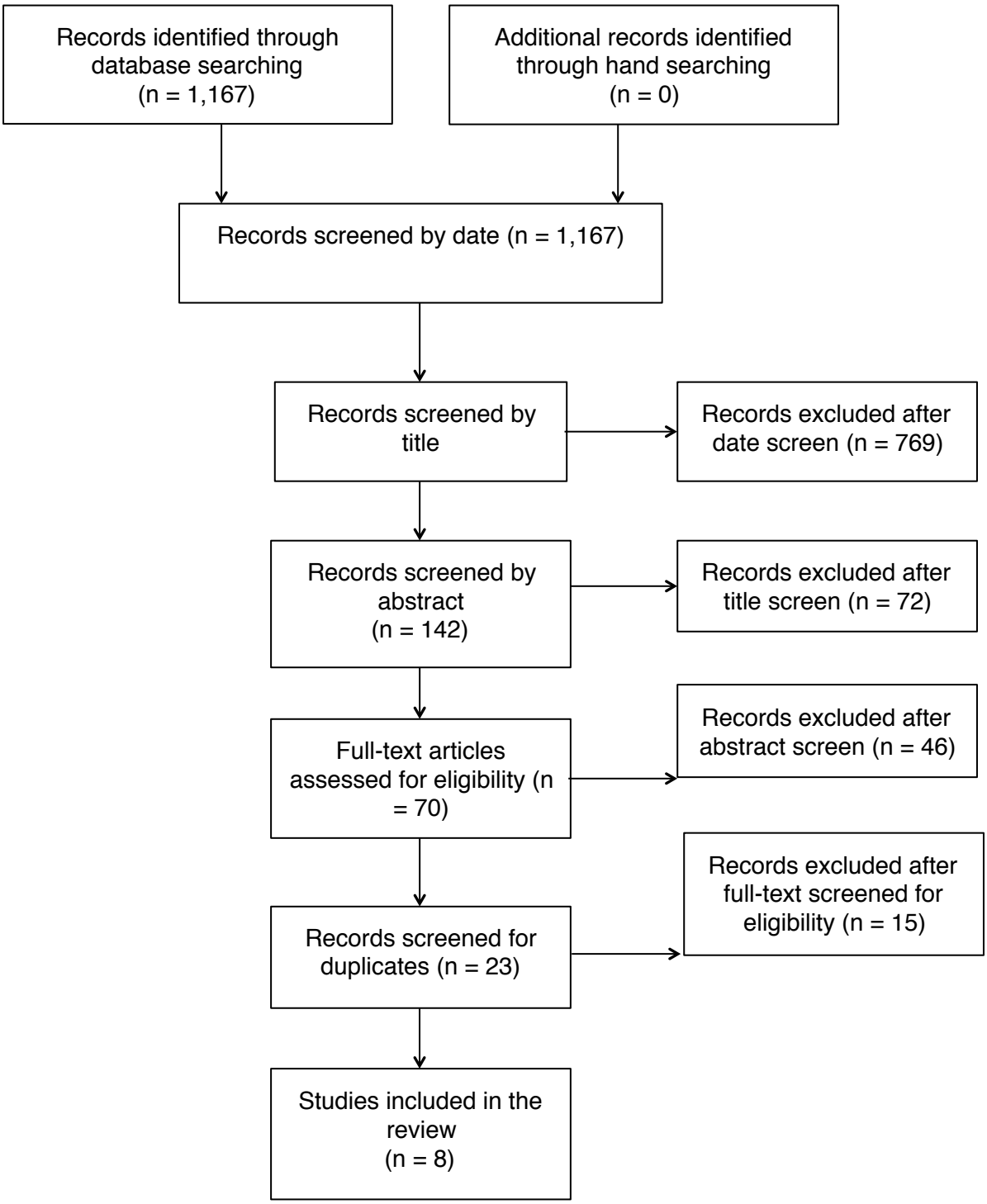

Figure 2: Weight change in intervention and control groups from baseline to end (kg)

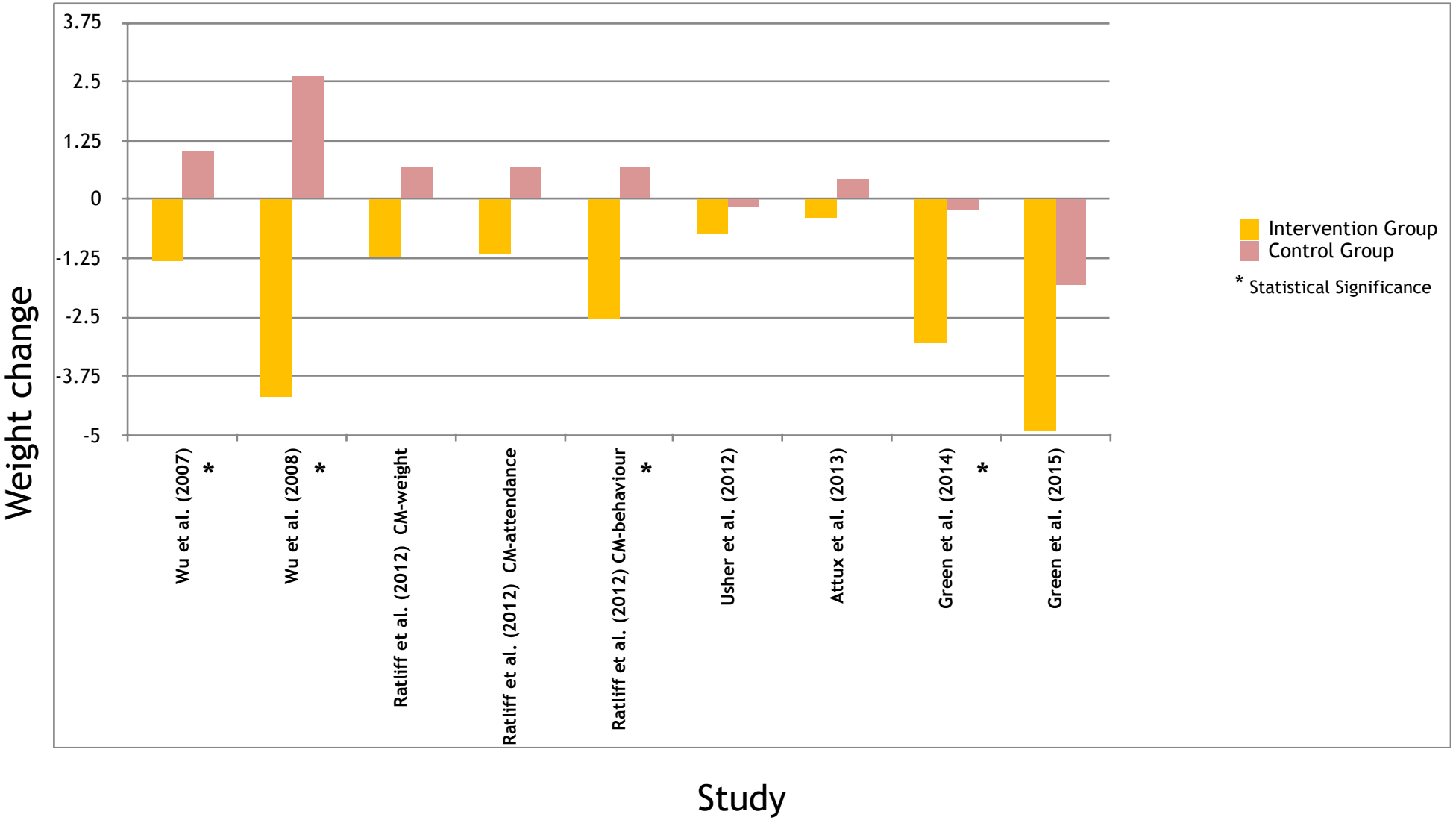

Figure 3 BMI change in intervention and control groups from baseline to end (kg/m^2)

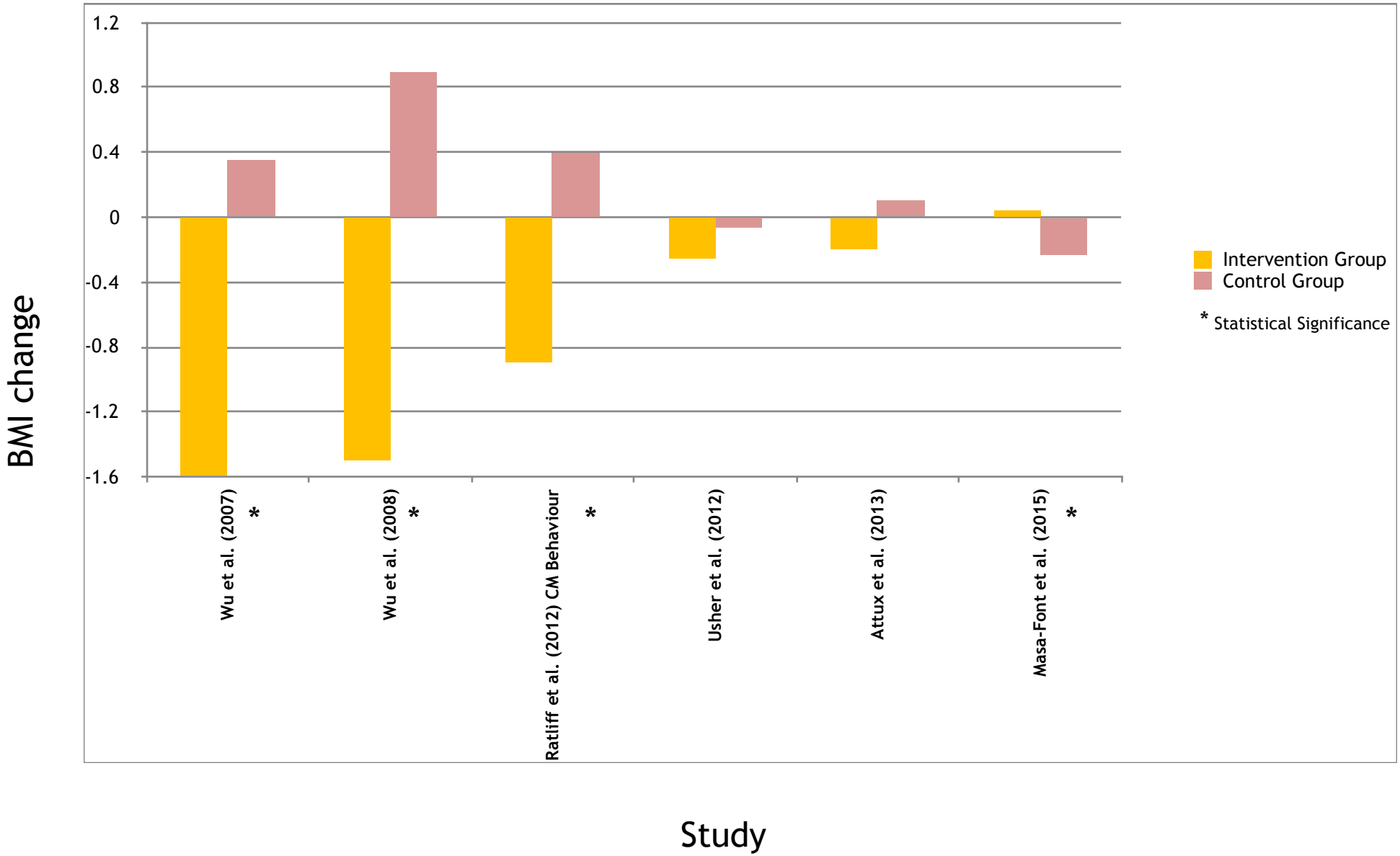

Figure 4: Waist circumference change in intervention and control groups from baseline to end (cm)